

Luteolin Exhibits Anti-Diabetic Effects by Increasing Oxidative Capacity and Regulating Anti-Oxidant Metabolism

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Abstract : Overweight and obesity have been linked to a low-grade chronic inflammatory response and an increased risk of developing metabolic syndrome including insulin resistance, type 2 diabetes mellitus and certain types of cancers. Luteolin is a dietary flavonoid with anti-inflammatory, anti-oxidant, anti-cancer and anti-diabetic properties. However, little is known about the detailed mechanism associated with the effect of luteolin on inflammation-related obesity and its complications. The aim of the present study was to reveal the anti-diabetic effect of luteolin in diet-induced obesity mice using “transcriptomics” tool. Thirty-nine male C57BL/6J mice (4-week-old) were randomly divided into 3 groups and were fed normal diet, high-fat diet (HFD, 20% fat) and HFD+0.005% (w/w) luteolin for 16 weeks. Luteolin improved insulin resistance, as measured by HOMA-IR and glucose tolerance, along with preservation action of pancreatic β -cells, compared to the HFD group. Luteolin was significantly decreased the levels of leptin and ghrelin that play a pivotal role in energy balance, and the macrophage low-grade inflammation marker sCD163 (soluble Cd antigen 163) in plasma. Activities of hepatic anti-oxidant enzymes (catalase and glutathione peroxidase) were increased, while the levels of plasma transaminase (GOT and GPT) and oxidative damage markers (hepatic mitochondria H₂O₂ and TBARS) were markedly decreased by luteolin supplementation. In addition, luteolin increased oxidative capacity and fatty acid utilization by presenting decrease in enzyme activities of citrate synthase, cytochrome C oxidase and β -hydroxyacyl CoA dehydrogenase and UCP3 gene expression compared to high-fat diet. Moreover, our microarray results of muscle also revealed down-regulated gene expressions associated with TCA cycle by HFD were reversed to normal level by luteolin treatment. Taken together, our results indicate that luteolin is one of bioactive components for improving insulin resistance by increasing oxidative capacity, modulating anti-oxidant metabolism and suppressing inflammatory signaling cascades in diet-induced obese mice. These results provide possible therapeutic targets for prevention and treatment of diet-induced obesity and its complications.

Keywords : anti-oxidant metabolism, diabetes, luteolin, oxidative capacity

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